Mifepristone

Cat. No.: HY-13683

CAS No.: 84371-65-3

Molecular Formula: $C_{29}H_{35}NO_2$

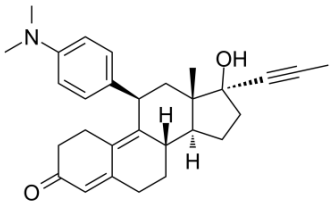
Molecular Weight: 429.59

Target: Progesterone Receptor; Glucocorticoid Receptor; NO Synthase; Autophagy

Pathway: Others; GPCR/G Protein; Immunology/Inflammation; Autophagy

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (232.78 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.3278 mL	11.6390 mL	23.2780 mL
5 mM	0.4656 mL	2.3278 mL	4.6556 mL
10 mM	0.2328 mL	1.1639 mL	2.3278 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.82 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Mifepristone (RU486) is a progesterone receptor (PR) and glucocorticoid receptor (GR) antagonist with IC_{50}s of 0.2 nM and 2.6 nM in in vitro assay[1].

IC_{50} & Target

IC50: 0.2 nM (progesterone receptor, in T47D cells), 2.6 nM (glucocorticoid receptor, in A549 cells)[1]

In Vitro

The discovery of the first competitive progesterone antagonist, Mifepristone, has stimulated an intense search for more potent and more selective antiprogestins[1]. Cell growth is evaluated after 4 days of exposure to Mifepristone at 10 μM, a

concentration close to the plasma concentration achievable in humans. The antiproliferative effect of NSC 119875 is potentiated when administered in combination with Mifepristone in HeLa cells. The IC_{50} of NSC 119875 in combination with Mifepristone is lower (14.2 μM) than that of NSC 119875 alone (34.2 μM) in HeLa cells with an approximately 2.5-fold difference. After treatment with Mifepristone, the accumulation of intracellular NSC 119875 in HeLa cells is 2-fold greater, representing a significant difference (p=0.009), compare with NSC 119875 alone from 0.79 to 1.52 μg/mg of protein[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

The cervix tumor xenograft models are treated with NSC 119875 alone, there is a tumor growth inhibition compare with control group. However, the tumor weight loss is even more significant ($p<0.05$) with the combination of NSC 119875 and Mifepristone at the doses used, showing a decrease of ~50% compared with the treatments alone by the end of the study[2]. Adult male Sprague-Dawley rats are subjected to a 4-day binge-like EtOH administration regimen (3 to 5 g/kg/i.g. every 8 hours designed to produce peak blood EtOH levels (BELs) of <300 mg/dL). Subgroups of animals receive s.c. injection of Mifepristone (20 or 40 mg/kg in peanut oil). Although Mifepristone produces no significant changes in behavior of EtOH-naïve animals, pretreatment with Mifepristone (40 mg/kg) significantly reducesthe severity of EtOH withdrawal. Asignificant interaction between diet and drug, $F(5,55)=3.92$, $p<0.05$, such that EtOH-treated animals receiving vehicle or 20 mg/kg of Mifepristone displayssignificantly more signs of EtOH withdrawal than does EtOH-naïve animals receiving the same drug treatment. Importantly, treatment with 40 mg/kg of Mifepristone significantly reduces the severity of EtOH withdrawal, in a dose-dependent manner[3].

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PROTOCOL

Cell Assay [2]

The HeLa and CaSki human cervical cancer cell lines are used. The effect of Mifepristone on proliferation of cells exposed to NSC 119875 is evaluated using the XTT assay. The assay is based on the cleavage of the yellow tetrazolium salt XTT to form an orange formazan dye by metabolically active cells. The procedure is as follows. Cells are seeded into 96-well plates; Costar at a density of 6×10^3 viable cells per well in 100 μL culture medium. At the end of treatment with NSC 119875 alone or the combination of NSC 119875 plus Mifepristone, 50 μL XTT is added to each well (final concentration 0.3 mg/mL), follow by incubation for 4 h in a humidified atmosphere containing 5% CO_2 at 37°C. The absorbance of the samples is measured spectrophotometrically at 492 nm using a microtiter plate ELISA reader[2].

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Animal Administration [2][3]

Mice[2]

Female Nude mice between 6-8 weeks of age are implanted subcutaneously with 6×10^6 HeLa cells in a flank. Once tumors are ~5×5 mm, the animals are pair-matched into treatment and control groups. Each group consist of 8 tumor-bearing mice. The intraperitoneal administration of drugs or vehicle begin on day 0. NSC 119875, as a single agent, is administered intraperitoneally at a dose of 3 mg/kg daily on days 1 through 3; the dose of Mifepristone, as a single agent, is 2 mg/kg/day subcutaneously for 3 days; in the combination study, the mice concurrently receive NSC 119875 on the same schedule, and Mifepristone at the same dose 3 days previous to the administration of NSC 119875. The control animals receive only the vehicle. After administration of the drugs, mice are weighed and the tumors are measured with a caliper twice weekly. The tumor weight is calculated. Experiment is conducted for 74 days, after which time all animals are weighed and humanely euthanized.

Rats[3]

Adult male Sprague-Dawley rats, weighing between 224 and 245 g upon arrival, are used. Mifepristone (20 or 40 mg/kg) or vehicle (peanut oil) are administered subcutaneously (s.c.) once daily following the 0800 administration of EtOH or control diet. Mifepristone is suspended in peanut oil and sonicated for 30 minutes at least 24 hours prior to injection, it is then stored at 4°C until needed. Suspension is vortexed for 10 to 15 minutes prior to and as needed throughout dosing.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2020 May 6;12(542):eaba0769.
- Arch Toxicol. 2020 Jun 3.
- Am J Physiol Cell Physiol. 2019 Sep 11.
- Sci Rep. 2017 Jul 26;7(1):6501.
- Am J Physiol Heart Circ Physiol. 2020 Jul 3.

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[1]. Jiang W, et al. New progesterone receptor antagonists: phosphorus-containing 11beta-aryl-substituted steroids. Bioorg Med Chem. 2006 Oct 1;14(19):6726-32.

[2]. Jurado R, et al. NSC 119875 cytotoxicity is increased by mifepristone in cervical carcinoma: an in vitro and in vivo study. Oncol Rep. 2009 Nov;22(5):1237-45.

[3]. Sharrett-Field L, et al. Mifepristone Pretreatment Reduces Ethanol Withdrawal Severity In Vivo. Alcohol Clin Exp Res. 2013 Aug;37(8):1417-23.

[4]. Yuehua You, et al. Progesterone Promotes Endothelial Nitric Oxide Synthase Expression Through Enhancing Nuclear Progesterone receptor-SP1 Formation. Am J Physiol Heart Circ Physiol. 2020 Jul 3.

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